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Original Paper

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Abstract

We used primary care data to retrospectively describe the entry, spread, and impact of COVID-19 in a remote rural community and the associated risk factors and challenges faced by the healthcare team. Generalized linear models were fitted to assess the relationship between age, sex, period, risk group status, symptom duration, post-COVID illness, and disease severity. Social network and cluster analyses were also used. The first six cases, including travel events and a social event in town, contributed to early infection spread. About 351 positive cases were recorded and 6% of patients experienced two COVID-19 episodes in the 2.5-year study period. Five space–time case clusters were identified. One case, linked with the social event, was particularly central in its contact network. The duration of disease symptoms was driven by gender, age, and risk factors. The probability of suffering severe disease increased with symptom duration and decreased over time. About 27% and 23% of individuals presented with residual symptoms and post-COVID illness, respectively. The probability of developing a post-COVID illness increased with age and the duration of COVID-associated symptoms. Carefully registered primary care data may help optimize infection prevention and control efforts and upscale local healthcare capacities in vulnerable rural communities.

Introduction

Research on COVID-19 epidemiology and impact has put the focus mainly on urban areas and large-scale or macro-level studies, while comparatively little research has addressed infection dynamics and impact in remote rural settings [1]. Differences between rural and urban areas that may affect COVID-19 spread, maintenance, and clinical impact include healthcare disparities, communication challenges, and higher population vulnerability [2]. Overall quality of life and mental health were perceived as being particularly impacted by COVID-19 pandemic in rural regions [1]. While these characteristics suggest increased risks in such settings, these areas do also benefit from some protective features such as a lower population density and contact rates [2], as well as a wider availability of open green spaces which has been shown to result in lower COVID-19 incidence and lower mortality [3].

In Spain, 82% of municipalities have fewer than 30,000 inhabitants and a population density lower than 100 inhabitants/km² [4]. These rural municipalities host 16% of the total population. One-third of the rural population lives in municipalities, each with fewer than 2,000 inhabitants. In the last decade, the registered urban population has increased by 2.1% in Spain, while the rural population has decreased by 7.1% due to emigration and deaths. Elsewhere, patients in rural areas have less access to medical care than those in urban areas [5], and socioeconomic inequalities as well as the place of residence influence the risk of COVID-19 [6]. The differences between urban and rural areas are also evidenced by psychotropic drug consumption, which increased during the COVID-19 pandemic, especially among women, the elderly, and in rural areas in relation to anxiety, insomnia, and depression [7].

Local primary healthcare provided through Primary Care Teams (EAP in Spanish) in urban and rural settings has been fundamental in managing the COVID-19 pandemic in Spain. The EAP initially assesses the severity of the patient, establishing who requires follow-up from primary care or transfer to hospital care [5]. However, primary healthcare underwent changes during the pandemic, mostly in relation to the digitization of assistance through telephone consultation, telematics assistance, electronic prescription, or telematics work disability reports [8].

We used detailed data from EAP Horcajo de Los Montes (Ciudad Real province, Spain) collected between 23 February 2020, and 11 July 2022, to describe the entry, spread, and impact of COVID-19 in a remote rural village and the challenges faced by the local EAP.

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Material and methods

Study site

Horcajo de los Montes (39°19'35"N 4°39'00"W) is a rural municipality of Ciudad Real province in the region Castilla-La Mancha. It is located 510 m above sea level in the centre of the Iberian Peninsula. The municipality has a total area of 208 km² and is partly included in Cabañeros National Park, a regional tourism hotspot. It is located 185 km from the national capital, Madrid, and 83 km from the provincial capital, Ciudad Real. The population is relatively sparse and ageing and has had a decreasing trend in numbers over the last decade with a 10% population loss; its current population density is 4.61 inhabitants/km². During the COVID-19 crisis, the population changed from 833 inhabitants in 2019 and 2020 to 821 in 2023 (−1.32%) (<https://www.ine.es/nomen2/index.do?accion=busquedaDesdeHome&nombrePoblacion=horcajo&x=10&y=6>; last accessed 06/12/2023). The mean age during the study period was 50.05 years with 38% of the residents over 65 years old (<https://www.ine.es/nomen2/index.do>; last access 02/21/2023).

Information sources and informed consent

We conducted a retrospective study analyzing sociodemographic and clinical variables of COVID-19 patients attended by the local EAP Horcajo de los Montes. Data were collected from 23 February 2020, to 11 July 2022, and integrated into a fully anonymized database. Data collection was accompanied by a study information sheet, and written informed consent was obtained from all participants. Subjects voluntarily participated in the study, and their data remained confidential and anonymous. All participants agreed to the use and publication of the findings. Ethical approval was not required as this study was based on responses to a questionnaire and clinical history, with privacy protection (Supplementary Material – Questionnaire). The data obtained were treated in accordance with both the Constitutional Law 3/2018, of 5 December, on the Protection of Personal Data and the Guarantee of Digital Rights, and the General Regulation on the Protection of Data of the European Union EU 2016/679 (RGPD), which came into force in Spain on 25 May 2018. The study complied fully with the guidelines and basic principles set by the Declaration of Helsinki.

Cases, contacts, and period definition

Case definition changed over time due to the initial constraints in accessing diagnostic tests. At the onset of the epidemic onset and confinement of subjects (from 23 February to 8 June 2020), cases were defined as patients who presented with acute respiratory symptoms associated with bilateral bronchopneumonia, fever, and general malaise, and who were either confirmed by PCR testing on hospital admission or remained as suspected cases before being subsequently confirmed COVID-19 positive by serology. On 9 June 2020, the Health Authorities requested the implementation of PCR tests in asymptomatic patients belonging to risk groups. This led to a change of the case definition the following day with the following classification: (I) any patient with a respiratory infection with cardinal symptoms of COVID-19 (loss of taste and smell, general malaise, fever for 7–10 days, and bronchopneumonia) and confirmed by PCR, (II) patients with symptoms of general malaise belonging to risk groups confirmed by PCR, and (III) risk contacts who, even if asymptomatic, were confirmed by PCR. On 5 October

2020, antigen tests were approved for contacts of positive patients and for populations at risk, as well as in outbreaks with high transmissibility. Both patients confirmed by PCR and those positive by a rapid antigen test were subsequently defined as cases. We defined a COVID-19 patient contact as any individual in direct contact with a confirmed patient (case) without a mask at less than 1.5 m and for more than 15 min in the 48 h prior to the confirmation of the case. Information on contacts was collected by questionnaires which were at times incomplete since some patients did not remember or wish to reveal details of their contacts.

The study was divided into four periods: period 1 “early cases and strict lockdown”; period 2 “interphase between strict lockdown and the start of vaccination”; period 3 “vaccination”; and period 4 “Omicron”.

Statistics

ANOVA was used for data with a normal distribution and Kruskal–Wallis tests for categorical data. A space–time permutation scan statistical model (SaTScan, version 9.6) was used to retrospectively analyze the spatial–temporal clustering of COVID-19 cases in the municipality from February 2020 to July 2022 [9]. The centroids of the residences were used for the coordinates of cases and clusters were identified using the log-likelihood ratio statistic. Monte Carlo simulations were used to evaluate the significance of the detected cluster *p*-value, and to ensure sufficient accuracy, the number of simulations was set to 999 [10].

As for social network characterization, four static social networks were constructed, one for each study period, using the *igraph* R package [11]. Networks included all patients belonging to the different spatial–temporal clusters obtained previously. The metrics of the nodes (i.e. degree and betweenness) and the network (i.e. size and density) were also estimated. The use of these parameters for a better understanding of the potential risk for disease spread had been recommended by previous studies [12]. Statistical differences in network and node metrics among periods were assessed using Kruskal–Wallis’ test with Dunn’s multiple comparison post hoc analyses [13].

For analyses, (i) the disease severity was defined according to the interim guidelines from the World Health Organization (WHO) [14] and was classified as asymptomatic, mild (slight clinical symptoms without imaging findings of pneumonia), moderate (fever or respiratory symptoms), and severe/critical (respiratory distress or failure, oxygen saturation < 93% at rest, shock, or other organ failure requiring intensive care unit treatment); (ii) the post-COVID illnesses were all conditions described after a COVID-19 episode, which might or might not be due to COVID-19; (iii) the risk group status was defined according to Rashedi *et al.* [15], considering risk factors: old age, obesity, asthma, hypertension, malnutrition, diabetes, pregnancy, cardiovascular disease, cancer, and others such as chronic obstructive pulmonary disease, chronic renal disease, or immunodeficiency.

For multivariable analyses, we used generalized linear models (GLMs). Firstly, collinearity among potential explanatory variables was explored, and then three sets of GLMs were fitted to assess the relationship between age, sex, period, risk group status, and the following response variables: (a) duration of symptoms (days; log-transformed) and (b) developing post-COVID illness (binomial response). The GLMs were fitted with a normal (a) or binomial (b) error distribution and the identity (a) or logit (b) link function, respectively. In addition, to assess the relationship between age, sex, period, risk group status, duration of COVID-associated

symptoms, and disease severity (as a response variable), a set of ordinal logistic regressions was fitted [16]. Model selection was based on Akaike information criterion (AIC) and Akaike weight (Wi) [17]. Models with differences in AIC lower than two ($\Delta\text{AIC} < 2$) were considered potential alternative models to the best model [18]. Once the final model/s was selected, the assumptions of the models were checked [19, 20]. GLMs were fitted in the library “stats” 4.1.3 version, whereas the ordinal logistic models were fitted with the library “AER” 1.2–10 version. Assumptions were checked with the libraries *ggfortify* 0.4.15 version and *brant* 0.3–0 version, respectively [21, 22]. All statistical analyses were performed in R version 4.0.2 [23].

Results

COVID-19 dynamics

In the 30 months following the onset of epidemic (between 23 February 2020, and 11 July 2022), 351 cases among 329 patients (39% of the total village population) were diagnosed with COVID-19. The minimum number of cases per 100,000 was 42,136. Three deaths were directly attributed to COVID-19 (0.36% mortality; 360/100 K mortality rate). Supplementary Figure S1 presents the COVID-19 case curves for the region Castilla-La Mancha and for the village, Horcajo de los Montes.

Among the positive cases, 51, 25, 27, and 234 cases were recorded in periods 1, 2, 3, and 4, respectively. All nine cases requiring intensive care occurred in period 1. The first six cases,

with symptom onset between 23rd February 2020, and 1st March 2020, included four travel events of village residents returning to their homes. During the first period, specifically in March, there was a large social event in the town and five patients with COVID-19 symptoms attended.

Table 1a shows the gender distribution and the mean age of COVID-19 cases, by period. Gender balance moved from a slight male bias in period 1 to a slight female bias in period 4. The mean age of cases in period 3 (26.7) was significantly younger than in others (46.6–52.8; ANOVA $F_{3, 347} = 9.3$; $P < 0.001$). All three deaths directly attributed to COVID-19 occurred during period 1. These fatalities were elderly patients who lived with their relatives at home and consulted too late in relation to the clinical symptoms since during the initial assessment the symptoms were already severe. Other causes of mortality included senescence and cancer. Fifteen patients required hospitalization (4.5%) with a mean hospital stay duration of 10 days (range: 1–53). These included 7 of 51 cases in period 1 (14%), 1 of 25 cases in period 2 (4%), 2 of 27 cases in period 3 (7%), and 5 of 234 cases in period 4 (2%).

Twenty-two of 329 patients (6%) experienced two COVID-19 episodes in the study period (Supplementary Figure S2). Twelve of these (60%) suffered the first infection during period 1 and a second episode during period 4, after the emergence of the Omicron variant. Patients with a single COVID-19 episode had a mean age of 45.4 years and included 150 males and 157 females; those with two episodes had a mean age of 46.6 years and included 10 males and 12 females. Patients with a single COVID-19 episode presented with signs for 10.7 ± 0.5 days and had a mean maximum disease

Table 1. Data obtained from registered COVID-19 cases in Horcajo de los Montes (Spain) by study period: (a) Gender distribution and mean age in years, (b) Mean number of contacts per case, (c) Number of cases integrating each cluster (members) and the number of contacts per cluster, divided into cluster members and non-members, in five space–time clusters, and (d) Network (size, density, and clustering coefficient) and node (degree and betweenness) metrics of temporal social networks constructed

| | Period 1 | Period 2 | Period 3 | Period 4 | Mean values | |
|--------------------------------------|----------------|-------------|-------------|----------------|----------------|-------------|
| a – Gender distribution and mean age | | | | | | |
| Sample size (Male/Female) | 35/30 | 13/12 | 13/14 | 109/125 | 42.50/45.30 | |
| Mean age (Male/Female) | 51.20/46.2 | 46.20/55.80 | 27.40/26 | 46.70/46.50 | 45.90/45.50 | |
| b – Mean number of contacts per case | | | | | | |
| | 4.21 ± 0.41 | 2.85 ± 0.28 | 3.81 ± 0.64 | 6.30 ± 0.22 | 4.29 ± 0.39 | |
| c – Clusters | | | | | | |
| | Cluster 1 | Cluster 2 | Cluster 3 | Cluster 4 | Cluster 5 | |
| N of members | 15 | 6 | 5 | 5 | 3 | 6.80 |
| N of contacts | 31 | 11 | 6 | 22 | 20 | 18 |
| Members (%) | 12 (39%) | 6 (54%) | 5 (83%) | 5 (23%) | 3 (15%) | 6.20 (43%) |
| Non-members (%) ^a | 19 (61%) | 5 (46%) | 1 (17%) | 17 (77%) | 17 (85%) | 11.80 (57%) |
| d – Network and node metrics | | | | | | |
| Size ^b | 245 | 54 | 81 | 1,420 | 450 | |
| Density ^c | 0.06 | 0.14 | 0.12 | 0.03 | 0.09 | |
| Clustering coefficient ^d | 0.45 | 0.79 | 0.86 | 0.39 | 0.62 | |
| Mean node degree ^e | 0.13 ± 0.01 | 0.28 ± 0.03 | 0.25 ± 0.05 | 0.06 ± 0.00 | 0.18 ± 0.03 | |
| Mean node betweenness ^f | 122.64 ± 36.11 | 1.90 ± 0.79 | 1.73 ± 0.79 | 828.10 ± 79.97 | 238.59 ± 29.42 | |

^aThe sum of individuals who belong to the remaining clusters.

^bTotal number of nodes and contacts that compound the network.

^cProportion of contacts observed in the network with respect to the total number of contacts that could possibly happen.

^dSummation of the proportion of nodes that are directly connected to another node.

^eNumber of adjacent edges of a specific node.

^fShortest paths of the network that pass through a specific node divided by the number of shortest paths of the network.

severity of 1.53 ± 0.04 . Individuals with repeating COVID-19 presented with signs for 16.7 ± 2 days and had a mean maximum disease severity of 1.86 ± 0.16 in the first episode, compared to 8.68 ± 2 and 1.13 ± 0.16 in the second one, respectively. Differences between single episode, first, and second episodes were significant (ANOVA for 'days with symptoms' $F_{2, 348} = 4.4$, $P = 0.012$; Kruskal–Wallis test for 'severity' H_2 , $N = 351 = 11.7$, $P = 0.002$). Residual symptoms were recorded in 4 of 22 (18%) patients with two COVID episodes, all with the first episode during period 1. Likewise, in 82 of 307 (27%) patients with a single COVID episode, 12 presented in period 1, 10 in period 2, 6 in period 3, and 54 in period 4. Five of 22 (23%) patients with two COVID-19 episodes suffered post-COVID illness, as did 63 of 307 (20%) patients with a single episode. Predisposing risk factors were present in 14 of 22 (63%) patients with two COVID-19 episodes and 176 of 307 (57%) of those with a single episode.

Contacts and spatial dynamics

A total of 64 of 329 COVID-19 patients (19%) had a recent travel history, including 33 immigrations and 31 resident returns. These included one international travel (Italy), 39 national, and 24 provincial movements (Supplementary Figure S3). In addition, there were five local cases without recent travel that were linked to visitors from Madrid not belonging to the Horcajo de los Montes EAP. Of the immigration or return movements, 19 took place in period 1, 10 in period 2, 10 in period 3, and 25 in period 4. However, the proportion of recorded movements declined in period 4 when no restrictions were in place.

The mean number of contacts per case by period and the five identified space–time clusters are shown in Table 1b and Figure 1, respectively. Differences between periods regarding the mean number of contacts per case were significant ($F_{3, 346} = 18$; $P < 0.01$). The larger number of contacts per case during period 1 was because the confinement to home started on 14 March 2020, while the first case was already symptomatic on 23 February 2020.

Table 1c shows the number of cases in each cluster and the number of contacts per cluster, divided into cluster members and

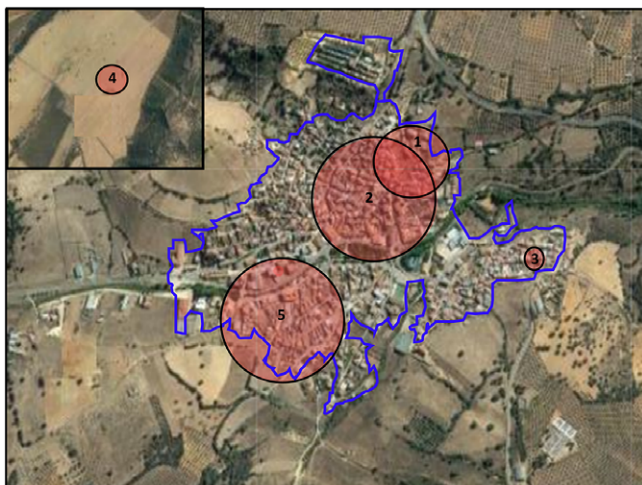


Figure 1. Space–time clusters of COVID-19 cases identified in Horcajo de los Montes (Spain) between February 2020 and July 2022. Cluster 1 occurred during period 1, probably linked to a social event (burial). Clusters 2 and 3 occurred during period 2, and clusters 4 (in a farm located 25 km from the village) and 5 during period 4. Cluster 2 occurred near cluster 1. Only clusters 4 and 5 had a link as one member of cluster 5 was a contact of one member of cluster 4.

non-members. On average, clusters were composed of 6.8 (range: 3–15) members and had 18 (range: 6–31) contacts. Direct links between clusters were likely only when they were close in time. Thus, a single direct link was found for clusters 4 and 5, where one member of cluster 5 was a contact of one member of cluster 4.

Of the contacts that were subsequently confirmed as new COVID-19 cases, contact networks were drawn for each phase and considering the case clusters (Figure 2). During period 1, patient 14 was particularly central in the contact network (degree = 0.66 vs. mean \pm standard error (SE): 0.13 ± 0.01 ; betweenness = 2035.97 vs. mean \pm SE: 122.64 ± 36.11). This patient was central to the large social event in March and the family home was located within the boundaries of cluster 1. Cluster 2 took place in the same part of the village as cluster 1, five months later. Clusters 3, 4, and 5 occurred in other parts of the municipality. Two clusters occurred during period 4, facilitated by the emergence of the highly transmissible Omicron variant. Node and network metrics are displayed in Table 1d. Nodes (patients) from period 1 and 4 networks showed significantly higher betweenness (Kruskal–Wallis $X^2 = 114.23$; $P < 0.01$) and lower degree values (Kruskal–Wallis $X^2 = 110.08$; $P < 0.01$) than those from periods 2 and 3 (Table 1).

Disease severity and long COVID-19

Duration of COVID-associated symptoms

According to the GLM selection procedure (Supplementary Table S1a), the duration of disease symptoms (days) was driven by gender, age, risk group, as well as the period (Supplementary Table S1a; $W_i = 0.51$). The duration of symptoms was longer during the first period in comparison to the rest of the study periods, being also greater in males, and in patients belonging to risk groups. Duration increased linearly with patient's age (Table 2a). The next best candidate model ($\Delta_i = 0.07$; $W_i = 0.49$) excluded the variable risk group status, which was not statistically significant in the first model.

Disease severity

We assessed the effect of the period and the duration of COVID-associated symptoms on disease severity (Supplementary Table S1c; $W_i = 100\%$). The probability of suffering from severe COVID-19 disease increased with the duration of symptoms and decreased over periods (Figure 3), whereas no differences were found for gender, age, or risk group status (Table 2c).

Post-COVID illness and symptoms

After the cure of COVID-19, 27% of the patients presented with residual symptoms. The most frequent was tiredness, followed by cough and dyspnea. In the trimester after cure, 23% of COVID-19 patients presented illnesses, mostly of a neurological type and more frequently in female patients over 60 years of age. The best model (Supplementary Table S1b; $W_i = 0.74$) revealed that the probability of developing post-COVID illness increased significantly with age and the duration of COVID-associated symptoms (Supplementary Figure S4; Table 2b).

COVID-19 impact on rural healthcare

This study could be carried out thanks to the continuity of the consultations despite the official closing times of the EAPs as well as

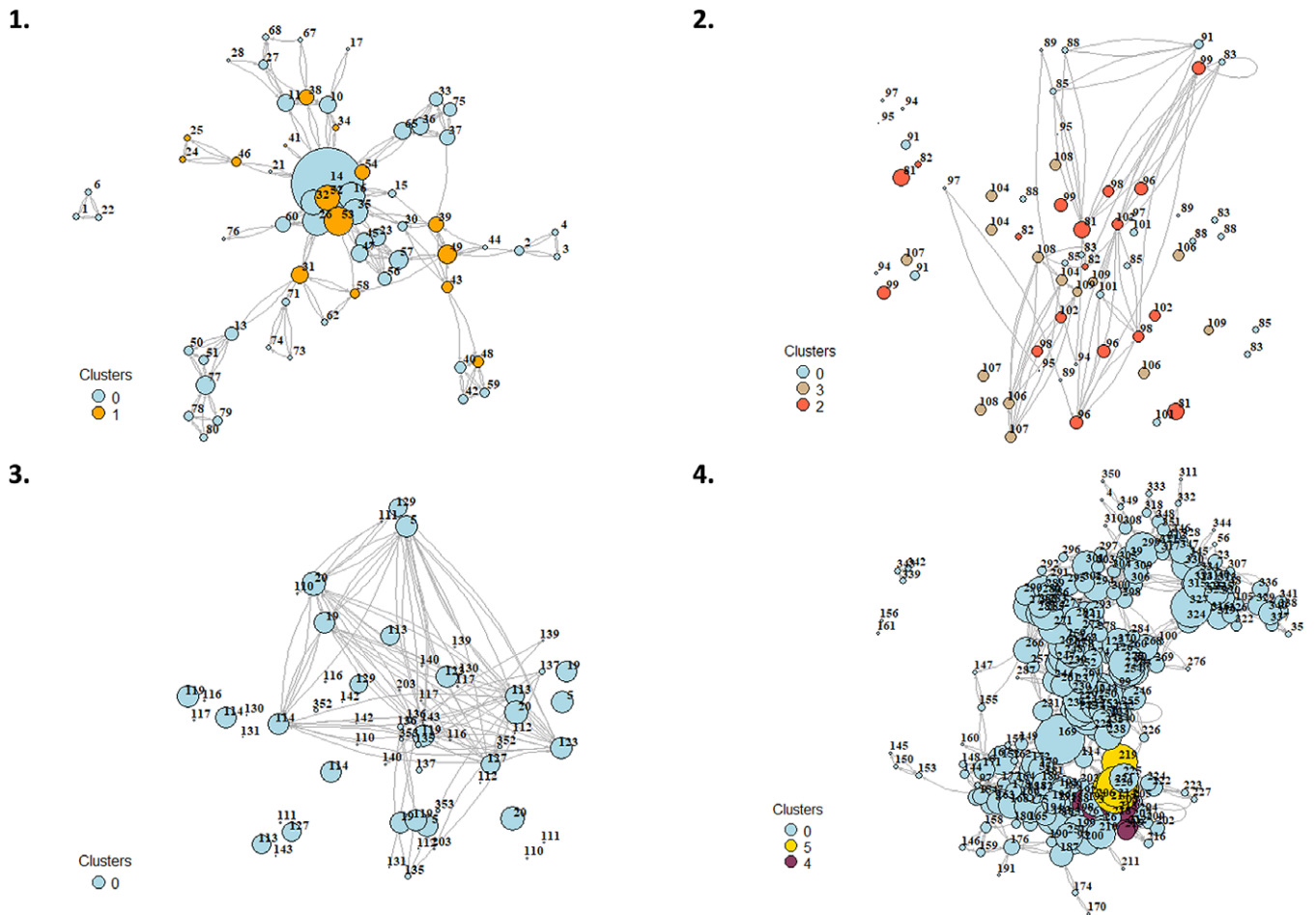


Figure 2. Contact networks of COVID-19 cases in Horcajo de los Montes (Spain), during the four defined periods (1–4). Colour codes indicate members of significant space–time clusters while 0 indicates cases not belonging to specific clusters. Node size is proportional to the degree of each patient. Edges represent known links between patients. The prominent role of case 14 is evident in period 1.

the personal attendance and follow-up of the suspect COVID-19 cases. The development of telemedicine led to changes in healthcare in Horcajo de los Montes and allowed for optimizing on-demand, scheduled, home and emergency appointments for patient care and telephone consultation. The EAP staff involved in providing local healthcare comprised a nurse and a medic, supported by an admin person. Supplementary Figure S5 displays the evolution of patients attended by the EAP staff during pandemic. With the arrival of the Omicron variant (period 4), clinical assistance temporarily increased by 20% in May 2022 reaching 24% in June 2022 before progressively returning to normal levels. Despite all constraints, there were no waiting lists for COVID-19 patients in the service except for an occasional wait of up to three days for administrative procedures.

Discussion

The COVID-19 pandemic and its impact in rural areas evidenced that future disaster mitigation policy actions need to consider the peculiarities of rural and remote areas, such as an old mean age, higher rates of chronic illness and, in consequence, high vulnerability along with limited healthcare capacities [2]. This study provided a detailed vision examination of the entry of SARS-

CoV-2, its spread, and maintenance, as well as its long-term consequences on health and the impact of COVID-19 on rural healthcare. A 2.5-year-long survey was carried out by a single observer, the primary care physician of Horcajo de los Montes, thereby minimizing bias in the clinical assessment of patients and avoiding observer bias.

The onset of local epidemic was possibly linked with national and international travel and with an important local event that facilitated multiple contacts across family units. Spain is a country with comparatively low internal migration levels. In 2020, however, due to the impact of COVID-19, the longstanding population decline from rural areas to core cities was suddenly reversed leading to net population gains in rural areas [24]. This is relevant in the context of COVID-19 epidemiology since immigrants from earlier infected urban areas might have contributed to outbreaks recorded in relatively isolated rural villages. Subsequently, the strict confinement regulations during period 1 and the less stringent ones during period 2 might have contributed to reducing infection transmission.

In Horcajo de los Montes, 39% of the village population was diagnosed with COVID-19 during the study period. This is far lower than some extreme values reported among unvaccinated adults in Bangladesh (62%; [25]) street adolescents in Togo (62%; [26]) or after the lifting of contact restrictions in Macao (70%; [27]),

Table 2. Parameters from the best models for the (a) duration of COVID-19 symptoms (days), (b) presence of post-COVID illness, and (c) disease severity in patients from Castilla-La Mancha (Spain) related to age, sex, period, risk group status, and duration of symptoms (log-transformed; in the case of the presence of post-COVID illness). Bold values are those considered statistically significant.

| a-Response variable: Duration of symptoms (days) | F df (x,y) | Estimate ± SD | P |
|-----------------------------------------------------|-------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------|
| Sex | 6.22 (1, 350) | Male: -0.10 ± 0.03 | <0.01 |
| Age | 33.41 (1, 350) | $<0.01 \pm <0.01$ | 0.01 |
| Period ^a | 29.05 (3, 350) | Period2: -0.49 ± 0.07 Period3: -0.31 ± 0.07 Period4: -0.39 ± 0.04 | <0.01 |
| Belonging to risk group | 2.02 (1, 350) | 0.06 ± 0.04 | 0.12 |
| b-Response variable: Presence of post-COVID illness | | | |
| Sex ^a | 2.68 (1, 350) | Male: -0.37 ± 0.28 | 0.10 |
| Age | 18.89 (1, 350) | $0.02 \pm <0.01$ | <0.01 |
| Duration of symptoms (days) – log transformed | 7.34 (1, 350) | 0.98 ± 0.36 | <0.01 |
| c-Response variable: Disease severity | | | |
| Sex ^a | | Male: -0.06 ± 0.21 | 0.79 |
| Age | | $0.01 \pm <0.01$ | 0.02 |
| Period ^a | | Period2: -3.37 ± 0.58 Period3: -2.22 ± 0.51 Period4: -3.39 ± 0.37 | <0.01 <0.01 <0.01 |

^aParameter estimates for the sex and period were calculated using females and first period as the reference.

all considerably higher than the officially recorded rate for Spain (29%; <https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/situacionActual.htm>; accessed 17 May 2023). The minimum number of cases per 100 K in our setting was 42,136, which exceeded the official cases/100 K (29,128) in Spain but was lower than the estimated cases/100 K reported for several countries worldwide [28, 29]. Diet and nutritional status of individuals have been reported to affect COVID-19 prevalence and disease course [30], particularly in populations with limited access to medical resources [31]. The relatively low incidence of COVID-19 in our municipality when compared to rural areas in developing countries may be influenced by a better nutritional status in these individuals [32].

Deaths directly attributed to COVID-19 were limited to three in our study, giving a mortality rate of 0.36% and a case fatality rate of 0.91 (3/329) considering the small population size (833 inhabitants in 2020). The corresponding mean mortality and case fatality rates recorded for Spain were 0.25% and 0.87, respectively [28, 29]. However, the small sample size did not allow reliable comparisons to be made with these data. The higher mean age and vulnerability of the rural village population might explain these results [28, 33]. Rapid diagnosis of the disease would reduce the number of fatal outcomes. This is a lesson for future outbreak events: rural health-care should be able to provide rapid access to advanced PCR diagnosis and health authorities should provide early and clear information to the population to avoid delays in adopting self-protective measures or requesting medical assistance after developing symptoms.

In our study cohort, the mean age of COVID-19 cases in period 3 was significantly younger than in other periods. One plausible explanation is confinement and vaccination since the former was no longer imposed in period 3, and younger persons would not yet have been vaccinated. Further, the summer period in Horcajo de los Montes is rich in social events involving young people, as evidenced by the finding that 6% of the patients became reinfecting during the whole study period. This is far higher than the mean frequency recorded for Europe (1.2%) and even higher than the corresponding global mean (4.2%; [34]). Reasons for this finding may include the careful follow-up of COVID-19 patients in the community and the high proportion of local patients with additional risk factors.

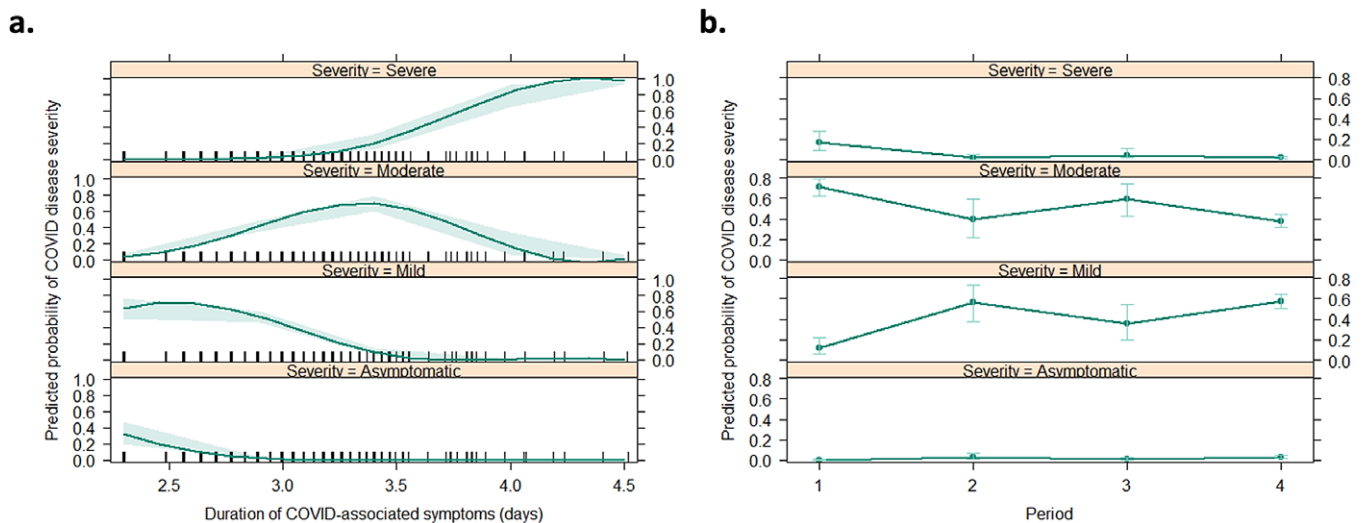


Figure 3. (a) Predicted probability (\pm confidence interval (CI) 95% represented by the shaded bands) of suffering from severe COVID-19 disease in Horcajo de los Montes, Spain, depending on symptom duration (days). (b) Predicted probability of severe COVID-19 (\pm 95% CI represented by the error bars) depending on the period.

The study of spatial clusters and social contact networks made it possible to visualize infection spread between cases in a community and to identify likely superspreaders (Figure 2). The collaboration of patients was essential for the early detection of cases. The social networks from the first and fourth periods were characterized by large sizes as well as by a low proportion of contacts (density) and patients directly connected to others (clustering coefficient; see Table 1). In these networks, the average node betweenness was higher since the lower number of contacts implies that each direct contact between two patients must necessarily go through certain individuals, who are considered central in the network and subsequently potential superspreaders [12]. In contrast, during the second and third periods, the patients were more directly connected to each other, so no individuals were identified as key to the disease spread.

Regarding other consequences on health, this dataset allowed the identification of several drivers explaining the duration of COVID-associated symptoms and the diagnosis of post-COVID illness. The duration of symptoms was driven by sex, age, risk group, as well as by the time period. Thus, a longer duration of disease-associated symptoms was related to older ages, female sex, and the presence of comorbidities [35–37]. The effect of the period and the fact that the duration of symptoms was higher during period 1 point to a positive effect of vaccination or variant-related differences in pathogenicity [38]. In the trimester after the cure of an initial episode, 23% of COVID-19 patients presented with illnesses, mostly of a neurological type, and more frequently in female patients over 60 years of age. Modelling revealed that the probability of developing post-COVID illness increased significantly with the duration of COVID-associated symptoms during the initial infection [39] (Figure 3).

Our study has several implications regarding rural healthcare. First, early interventions carried out in the community were essential to limit infection spread. These were facilitated by face-to-face contact with patients both at the time of suspicion of infection and after confirmation and treatment. The teleconsultation systems were also relevant for the follow-up of patients and their contacts, quickly reporting if there was clinical worsening or confirming cure when the patient reported being asymptomatic and, in the case of contacts, inviting them to the consultation if symptoms developed, thus facilitating early diagnosis and eventually confinement. These measures facilitated the containment of patients by primary care, largely avoiding the need for expensive second-level care (i.e. in hospitals).

Telemedicine optimized time budgets, reducing the time to solve bureaucratic issues and gaining time for face-to-face patient care. Waiting lists should only be established for administrative, bureaucratic, or delayable chronic pathology consultations. The availability of at least 10–15 min per clinical patient visit is essential for disease control and surveillance. It is important to note that in Spain, healthcare is universal and that some primary care indicators, such as the number of patients per medic, are better in small villages than in large cities. Consequently, time per patient will, in general, be greater in small villages than in cities. Thus, there should be no waiting list for the care of the sick patient in primary care consultation and de-bureaucratization of primary care should be a priority.

Personalized, ongoing patient care by the same primary care physician strengthens the doctor-patient relationship and mutual trust. The close medic-to-patient relationship in the Horcajo de los Montes might explain, in addition to the population age structure, the low hesitation about coronavirus vaccines observed

among local inhabitants (2,3% vaccine refusal, compared to 6.5% in Spain [40]).

Conclusion

This detailed survey in Horcajo de los Montes confirms that infection prevention and control efforts including healthcare capacity should be locally customized and scaled up in vulnerable rural areas [41, 42]. Further, it shows how carefully registered primary care data can provide useful insights into infection dynamics and disease impacts, especially in small rural communities.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0950268823001759>.

Data availability statement. The data that support the findings of this study are openly available upon reasonable request.

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Competing interest. The authors declare none.

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